

**ATTORNEY DOCKET NO. 14114.0331U2
APPLICATION NO. 10/018,627**

Remarks

Claims 1-12 are pending. Claim 12 has been withdrawn as being drawn to a non-elected invention. Claims 1-11 are rejected.

35 U.S.C. § 112, ¶ 2

1. Claims 1-11 are rejected under 35 U.S.C. § 112, ¶ 1 for allegedly failing to comply with the enablement requirement. In particular the claims have been rejected because the extent of public availability for the viral deposit is allegedly unknown. Applicant respectfully traverses this rejection. As noted on page 18, lines 18-19, the deposit was made with the ATCC (ATCC Accession No. VR-2635), an International Deposit Authority (IDA), under terms of the Budapest Treaty on December 2, 1998. Applicants remind the examiner that according to 37 C.F.R. 1.803, an IDA is an acceptable depository as established under the Budapest Treaty. Furthermore, the Budapest Treaty sets a term of at least 30 years from the date of deposit and at least 5 years after the most recent request, which is the requirement established under 37 C.F.R. 1.806. MPEP 2408 states that “[u]nless applicant indicates that the deposit has been made under the Budapest Treaty, applicant must indicate the term for which the deposit has been made.” As applicants have clearly referenced that the deposit was made under the Budapest Treaty on page 18, lines 18-19, and have stated the date of deposit, name of the depository, and assigned accession number, no affidavit or declaration of term length is needed (MPEP 2408). In any case, applicants herewith assure the patent office that all restrictions imposed by the depositor on the

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availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. Thus, withdrawal of this objection is respectfully requested..

2. Claims 3-6 and 7-11 are rejected under 35 U.S.C. § 112, ¶ 1 for allegedly failing to comply with the enablement requirement. In particular claims 3-6 and 7-11 have been rejected for allegedly failing to teach how to make viruses with heterologous inserts, how the virus will kill dividing cells, as well as, how the virus can inhibit tumor formation or growth. Applicants respectfully traverse the rejection. *In re Buchner* (929 F.2d 660,661) establishes that applicants are not required teach what is well known in the art. As such, applicants have not failed the enablement requirement by not disclosing basic knowledge as to spumavirus infections, essential genes of the virus, or well known molecular biological techniques.

For example, the Examiner states that “[s]ince the virus does not cause disease in humans and humans contain dividing cells, it is not clear how the same virus can not cause disease in one subject and kill dividing cells in another.” Applicants respectfully submit that the Examiner has confused terminology understood by those skilled in the art. Specifically, the Examiner is under the mistaken impression that killing dividing cells and not causing disease are mutually exclusive. This is incorrect. The term “disease” is understood in the art to mean any deviation from or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of symptoms and signs (emphasis added) and whose etiology, pathology, and prognosis may be known or unknown (p481 Dorland’s Illustrated Medical Dictionary 27th ed. E. J. Taylor, editor (1988) W.B. Saunders Co. Philadelphia, PA). This understanding is key to the understanding of the present

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invention. The presence of an infection, is not necessarily the presence of disease. Infections can and do exist in many viral situations without causing disease. For example, nearly 90% of the human species worldwide is infected with Herpes Simplex Virus-1. For many, this virus escapes any notice having no evident symptoms or pathology. However, in 10% of the infected individuals disease is evident in the presence of cold sores. Similarly, it is well known in the art that spumaviruses have not been associated with disease.

However, spumaviral infection of a cell will result in the infected cell being killed. Specifically, the egress of the virion from the infected cell results in the destruction of the cell. But, viral exit should not be confused with disease, for as the lysis of the infected cell would indeed be a cytopathic effect of the spumavirus infection, this is not associated with any symptom or greater pathology. Therefore, even though a cell may be killed as a result of a spumavirus infection, the infected subject will have no symptoms due to the infection and therefore no disease. As this is a basic knowledge of spumavirus infections (p 405 Heneine et al (1998) *Nature Med.* 4(4):403-7) under *In re Buchner*, applicants have not failed the enablement requirement of 35 USC 112 by not teaching this aspect of the virus.

The Examiner also alleges the applicants have failed to enable the how to make mutant viruses with heterologous inserts. In support of this proposition the Examiner puts forth Schenk as providing evidence that "foamy viruses are complex and have specific requirements in the[ir] genome to be infectious and that certain functions must be maintained." Applicants respectfully traverse this rejection. The Examiner uses this statement to imply that molecular manipulations of the spumavirus genome would be expected to be difficult or to have unpredictable results.

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This is not what Schenk teaches. In the context used by Schenk, "complex" does not mean difficult to understand, but rather, refers to a genome with many genes and interactions as opposed to a simple genome with few genes. Spumaviruses have a complex genome (composed of many genes), but Schenk does not teach or suggest that the genome is difficult to understand or that attempts to use the virus would lead to undue experimentation. Indeed, Schenk clearly teaches on page 1593 that *Tas*, LTR, and IP are all known to be required for spumavirus gene expression and were shown as such by Rethwilm in 1995 and Linial in 1999. Schenk shows a strong knowledge of the viral genome listing *Env*, *Gag*, *Pol*, *bel-1*, and *bel-2* genes in addition to knowledge of *Tas*, LTR, and IP. It is also clear the Schenk knows where these genes would be in a spumavirus (Fig 1). Lastly, despite knowing that the *Tas* is required for gene expression, Schenk is able to create a *Tas* negative mutant virus that is replication competent using techniques common in the art (page 1594). Schenk indicates that the interruption of the interaction between *Tas*, LTR, and IP is the reason for reduced titers in the mutant virus. Moreover, the key point of Schenk is that a replication competent mutant can be made despite the deletion of a known required gene (i.e. *Tas*). Thus, Schenk actually contradicts the Examiner's assertion. Schenk is evidence that the spumavirus genome is well known and understood and can be manipulated using art recognized routine techniques.

Moreover, it is not required of the present application to teach techniques of molecular biology that are in everyday use and can be found in any molecular biology lab manual (e.g. Maniatis). Clearly the Examiner cannot reject the present application for not teaching that which was previously known (i.e. how mutant viruses with heterologous inserts can be made). The

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making of recombinant viruses is well known in the art, and as such the routine details need not be taught in the present application.

Furthermore, the applicants have disclosed in detail on page 16, lines 31-page 17 line 31, both how tumor or other rapidly dividing cells will be infected and killed, such killing of tumor cells necessarily inhibiting growth or formation. This teaching, read in light of what was generally known about other spumaviruses, provides guidance to the skilled person as to how to make and use the present spumavirus with an insert.

The Examiner alleges that there is no evidence, guidance, or direction as to how the virus kills dividing cells or is effective against tumors or other related diseases. The Examiner then states that the specification is not commensurate with the scope of the claims in that it discloses that a "virus could be made that only binds certain receptors (page 18, line 1) and that viruses may be administered for cancer treatment." Applicants respectfully point out to the Examiner that spumaviruses only infect dividing cells. On page 16, lines 31-page 17 line 9, and page 17, lines 29-31, it is clear that the virus specifically infects dividing cells and even though non-dividing cells may become infected, nonproductive infections will result. Only dividing cells will be killed as a result of the infection. As this feature is a natural facet of the spumavirus lifecycle, it is not necessary for the specification to explain the mechanism of how to accomplish what is shown will naturally occur. Also as stated previously, it is not necessary for the application to teach what is known in the art. That is, that spumaviruses infect dividing cells. As tumors are, by definition, unregulated rapidly dividing cells, a spumavirus would easily infect the tumor cells and kill the cells upon exit. With regards to the Examiner's statements regarding

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page 18, line 1 and page 18, line 8, the specification describes alterations that can be made to the virus to specifically direct infection, more specifically, a recombinant modification to select only specific dividing cells with certain types of cellular receptors. This sentence does not mean, as the Examiner asserts, that dividing cells will only be infected if a recombinant virus is made specific for attachment to certain types of cellular receptors. Furthermore, the Examiner has interpreted the word "may" on page 18, line 8 to mean might or could possibly be used for cancer. However, "may" in this sentence is understood to mean that it is permissible to administer the virus to a host to treat cancer.

Because the Examiner has failed to establish that any technique needed or the required knowledge of the virus was outside the knowledge in the art when read in combination with the teachings of the present application, applicants believe this rejection to be overcome and respectfully request its withdrawal.

3. Claims 3-6 and 7-11 are rejected under 35 U.S.C. § 112, ¶ 1 for allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that an SFVHu-6 with an insert and a method of killing dividing cells, *in vivo* and *in vitro* with the SFVHu-6 of the invention as well as inhibiting tumor formation or growth has not been described in such a way as to reasonably convey to someone of skill in the art that the applicants are in possession of the invention. The Examiner then cites *Vas-Cath Inc. v. Mahurkar* ((CAFC, 1991) 19 USPQ2d 1111) to provide a legal basis for this position. Applicants respectfully traverse the rejection. Applicants have provided detailed nucleic acid sequences for the disclosed virus. Furthermore, the applicants have disclosed in detail on page 16, lines 31-page

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17 line 31, both how tumor or other rapidly dividing cells will be infected and killed, such killing of tumor cells necessarily inhibiting growth or formation. Also, Vas-Cath makes clear that the written description is to be interpreted by those of skill in the art. Moreover, *In re Wertheim* (541 F.2d 257, 263) states that "the PTO has the initial burden of presenting evidence or reasons why persons of skill in the art would not recognize in the disclosure a description of the invention as defined by the claims." Applicants believe that one of skill in the art reading the specification with the knowledge of the art would easily recognize applicants were in possession of the invention. Specifically, one of skill in the art would know how to make a recombinant virus and knowing about the spumavirus genome would readily understand where genes could be inserted or deleted. As discussed above, having knowledge of the spumavirus lifecycle one of skill in the art would know that the virus would infect and kill dividing cells and understand how this could be used against tumors. Moreover, the applicants believe the Examiner has not met the burden of showing why one of skill in the art would not recognize applicants had possession of the invention as described, but merely asserted such. Applicants believe they have overcome this rejection and respectfully request it be withdrawn.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.